

ANTI-NOCICEPTIVE POTENTIALS OF *ARTOCARPUS ALTILIS* (BREADFRUIT) ON WISTAR RATS IN THERMAL MODEL OF PAIN STUDY

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ABSTRACT

This study evaluated the effect of methanolic extract of *Artocarpus altilis* on thermal model of pain in albino wistar rats. The study was carried out on twenty-five (25) albino wistar rats of fifteen males and ten females, weighing 200-250g. The Eddy's hot plate technique as a thermal model for nociception was adopted. The LD50 value was determined as 2800mg/kg using Karber's method. Standard doses were taken below the LD50 value as 100mg/kg, 200mg/kg and 300mg/kg of the methanol extract of the plant. The albino wistar rats were divided into five groups with each group containing five animals (3 males and 2 females) each. Group A served as control group and were administered 5ml of distilled water orally. Groups B, C and D received 100mg/kg, 200mg/kg and 300mg/kg doses of MEAA orally. However, group E 200mg/kg of aspirin orally, as a reference drug. The different temperatures ($30\pm 0.5^{\circ}\text{C}$, $45\pm 0.5^{\circ}\text{C}$ and $60\pm 0.5^{\circ}\text{C}$) set on an electric hot plate were compared among the test and control groups. The result showed that MEAA seeds administered orally showed level of significance ($p < 0.05$) analgesic effect on nociceptive stimuli as initiated by a thermal panel at the set temperatures. Though the analgesic effect of aspirin was seen to be more potent than that noticed in the MEAA groups, but the analgesic effects in the MEAA treated groups was in a much similar fashion to that of aspirin. Therefore, the present study submits that MEAA possess significant analgesic effect on the biological system.

Key words: Methanol extract, *Artocarpusaltilis*, Pain, Thermal model.

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INTRODUCTION

Inflammation and pain are some of the most frequent reasons patients seek medical

advice and treatment. Of course, inflammation and pain depict important medical and economic costs for the community.^[1] Pain, has been described as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.^[2] The feeling of pain

constitutes an alarm that helps protect the organism: it both triggers reactions and induces learned avoidance behaviours, which may decrease whatever is causing the pain and, as a result, may limit the (potentially) damaging consequences.

Despite the proven efficacy in alleviating symptoms and providing relief by current therapies, virtually all have considerable side effects.^[3] Anti-inflammatory drugs or agents including NSAIDs and steroids have appreciable gastrointestinal and renal impacts amongst other side effects. Analgesics, other than NSAIDs, for example, opioids also cause remarkable adverse effects like respiratory depression, emesis, constipation, tolerance and addiction. These challenges of current therapy together with the fact that many patients especially pain sufferers are not satisfied with their pain care, thus making them resort to alternative analgesic and anti-inflammatory agents that can render more effective relief to their conditions.^[3] In our area, due to the availability and accessibility to plant products and herbs, the alternative therapies to orthodox treatments are always these plant products and herbs.^[4, 5]

MATERIALS AND METHOD

Plant Materials

Artocarpusaltilis (breadfruit) were purchased from Port-Harcourt Central Fruit market. The fruits were identified and confirmed for use by a botanist in the University Of Port Harcourt herbarium. The fruits were then ground into powder form. The powdered *Artocarpusaltilis* was soaked

with 100% methanol in a glass jar container and was left for a period of 72 hours. Thereafter, the mixture was decanted using filter paper and then evaporated using rotatory evaporator. The extract was evaporated to semi-solid form and then preserved in a refrigerator, from which appropriate quantity was collected to formulate the various administered doses.^[6]

Experimental Animals

A total of twenty-five male and female albino wistar rats were used for the experiment. The albino rats were acquired from the animal house of Faculty of Basic Medical Sciences, University of Port Harcourt. The animals were kept in ventilated wooden cages at room temperature (24-25⁰C). The animals were allowed to acclimatize for a period of three weeks with access to water. During the period of acclimatization, they were fed with finishers feed and their beddings were always changed after two days. After the three weeks of acclimatization, the animals were grouped into five with five rats (3 males and 2 females) each. They include GROUP A- Control (Fed with only normal feed and distilled water)

GROUP B- Administered with c of the extract of *Artocarpusaltilis*.

GROUP C- Administered with 200mg/kg of the extract of *Artocarpusaltilis*.

GROUP D- Administered with 300mg/kg of the extract *Artocarpusaltilis*.

GROUP E- Reference drug (aspirin).

Notably, the control and reference groups received 10 ml distilled water and 300mg/kg of aspirin; while the three test groups received 100mg/kg, 200mg/kg and

300mg/kg of *Artocarpusaltilis* respectively.

The route of administration was oral.

Acute Toxicity Test

To determine the lethal dose of methanol extract of *Artocarpusaltilis* to be administered to experimental animals, series of dose dependent test were carried out and are presented in the in the table below

Media	Qty in Grams	Observation	no of death	Lethal Concentration	Lethal Dose	Safe Dose
Methanol	0.5	Normal, Stable,	not sig.	>1g (1,2,3g) Etc.	0.5g	100, 200, 300mg or less per kg b.w.
	1	Sluggish, tail wagging, anorexic, Death	sig			
	2-3	Neurological deficit, slow, death	sig			

Thermal Pain Model Study Using Eddy's Hot Plate Test

Thirty minutes after administration of the respective substances in the different groups, the rats were placed on an electric metal hot plate maintained at $30 \pm 0.5^{\circ}\text{C}$, $45 \pm 0.5^{\circ}\text{C}$ and $60 \pm 0.5^{\circ}\text{C}$.^[7] A laboratory thermometer was used to get the accurate temperature of the metal hot plate for the test. A cut off time of fifteen seconds was maintained to avoid thermal injury. The reaction time (seconds), characterized by either licking the paw or jumping off the hot plate was noted. The response of *Artocarpusaltilis* and aspirin treated groups were compared with those animals in the control group (distilled water administered animals). The reaction time obtained for each group of the animals at different hot plate temperatures was

recorded and the average expressed as the mean time spent on the hot plate.^[8] The protection of the animals from the thermal stimuli was calculated using the formula:

Percentage protection (%) =

Latency (test) - Latency (control) × 100

RESULTS

The result in table 3.1 shows that five milliliters (5ml) of distilled water administered animals had significant ($P < 0.05$) inhibition of thermally induced pain at all temperatures used in the study (between 30°C and 45°C , 30°C and 60°C). However it was not significant between temperature 45°C and 60°C .

Table 1: Inhibition of thermally induced pain in Group A animals administered with 5ml of distilled water.

Parameter	Test Temperature (°C)		
	30	45	60
Percentage Protection (%)	4.54± 0.311 ^b	1.66±0.163 ^{a, b}	1.97±1.251 ^a

Each value represents Mean ± SEM (standard error of mean) of five replicates of study animals. ^a represents significant difference at p<0.05 when comparing 30°C test temperature to others. ^b represents significant difference at p<0.05 when comparing 45°C test temperature to others.

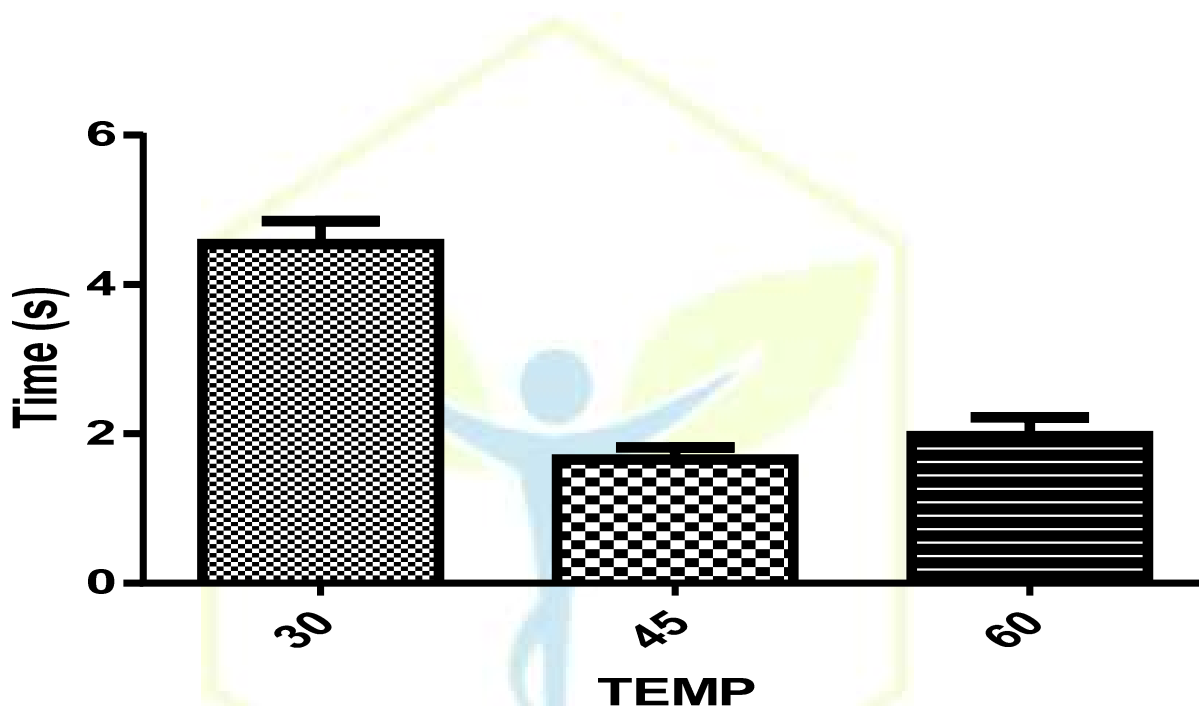


Figure 1: Graphical representation of the inhibition of thermally induced pain in Group A animals administered with 5ml of distilled water

Table 2: Inhibition of thermally induced pain in Group B animals administered with 100mg/kg of methanol extract of *Artocarpus altilis*.

Parameter	Test Temperature (°C)		
	30	45	60
Percentage Protection (%)	2.27±0.182 ^b	1.206±0.086 ^{a, b}	1.274±0.165 ^a

Each value represents Mean ± SEM (standard error of mean) of five replicates of study animals. ^a represents significant difference at p<0.05 when comparing 30°C test temperature to others. ^b represents significant difference at p<0.05 when comparing 45°C test temperature to others.

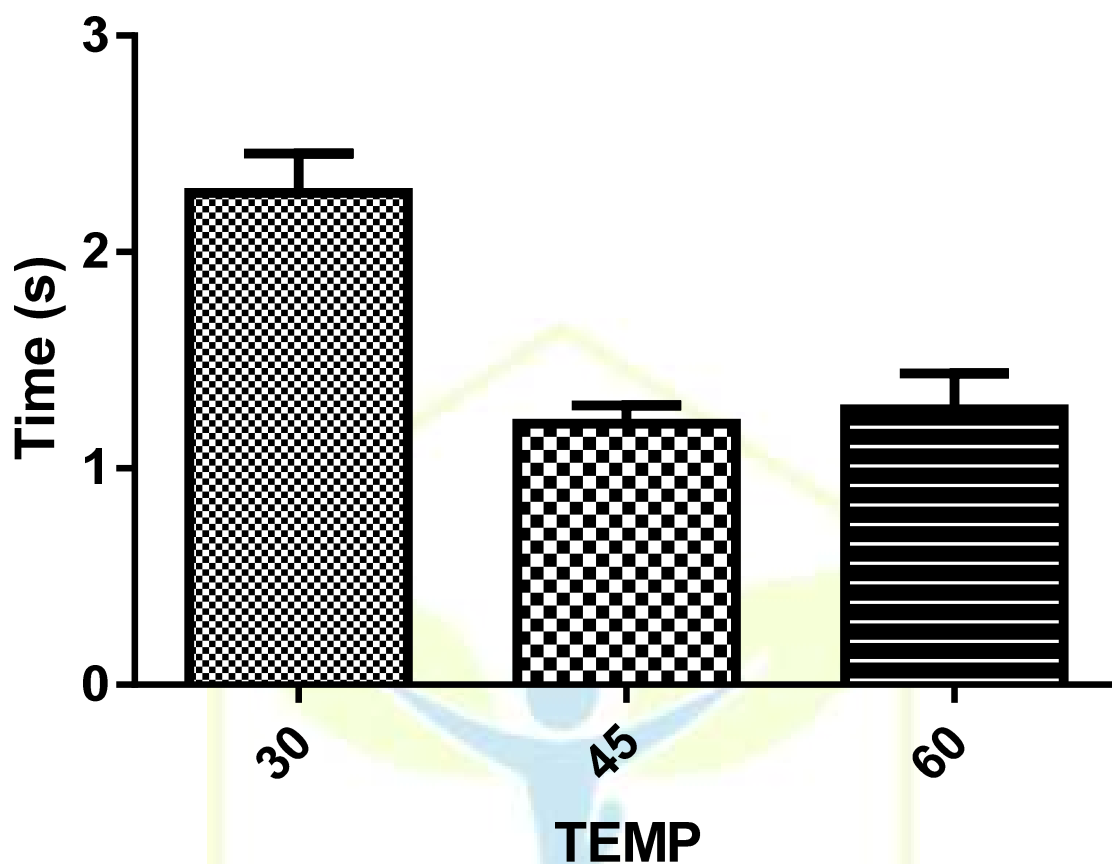


Figure 2: Graphical representation of the inhibition of thermally induced pain in Group B animals administered with 100mg/kg of methanol extract of *Artocarpus altilis*.

Table 3: Inhibition of thermally induced pain in Group C animals administered with 200mg/kg of methanol extract of *Artocarpus altilis*.

Parameter	Test Temperature (°C)		
	30	45	60
Percentage Protection (%)	2.972±0.068 ^{b, c}	2.032±0.143 ^{a, b, c}	1.310±0.053 ^{a, c}

Each value represents Mean ± SEM (standard error of mean) of five replicates of study animals. ^a represents significant difference at p<0.05 when comparing 30°C test temperature to others. ^b represents significant difference at p<0.05 when comparing 45°C test temperature to others. ^c represents significant difference at p<0.05 when comparing 60°C test temperature to others.

The 200mg methanol extract of *Artocarpusaltilis* significantly (P<0.05) inhibited thermally induced pain at all the hot plate temperatures (30⁰c, 45⁰c and 60⁰c).

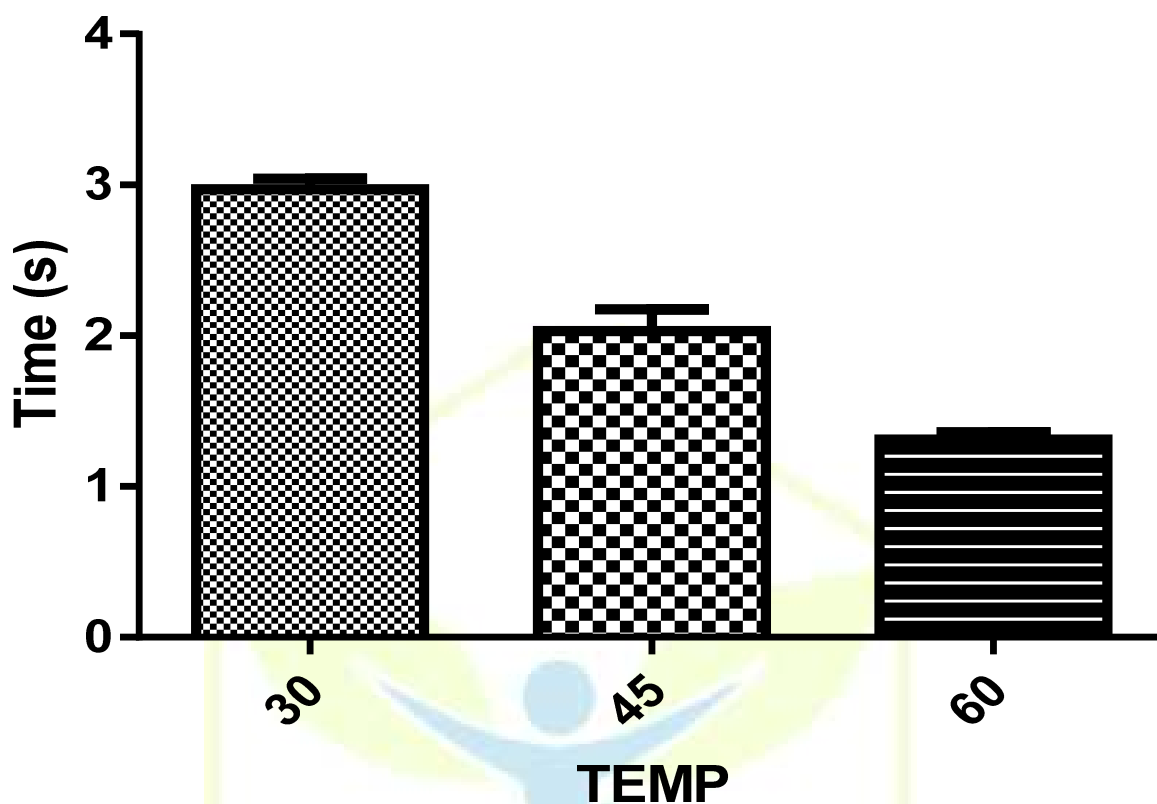


Figure 3: Graphical representation of the inhibition of thermally induced pain in Group C animals administered with 200mg/kg of methanol extract of *Artocarpus altilis*.

Table 4: Inhibition of thermally induced pain in Group D animals administered with 300mg/kg of methanol extract of *Artocarpus altilis*.

Parameter	Test Temperature (°C)		
	30	45	60
Percentage Protection (%)	4.150±0.07 ^b	2.604±0.184 ^{a, b}	1.994±0.163 ^a

Each value represents Mean ± SEM (standard error of mean) of five replicates of study animals. ^a represents significant difference at p<0.05 when comparing 30°C test temperature to others. ^b represents significant difference at p<0.05 when comparing 45°C test temperature to others.

The 300mg/kg methanol extract of *Artocarpus altilis* significantly (P<0.05) inhibited thermally induced pain at all the temperatures consider in this study (30^oc, 45^oc and 60^oc).

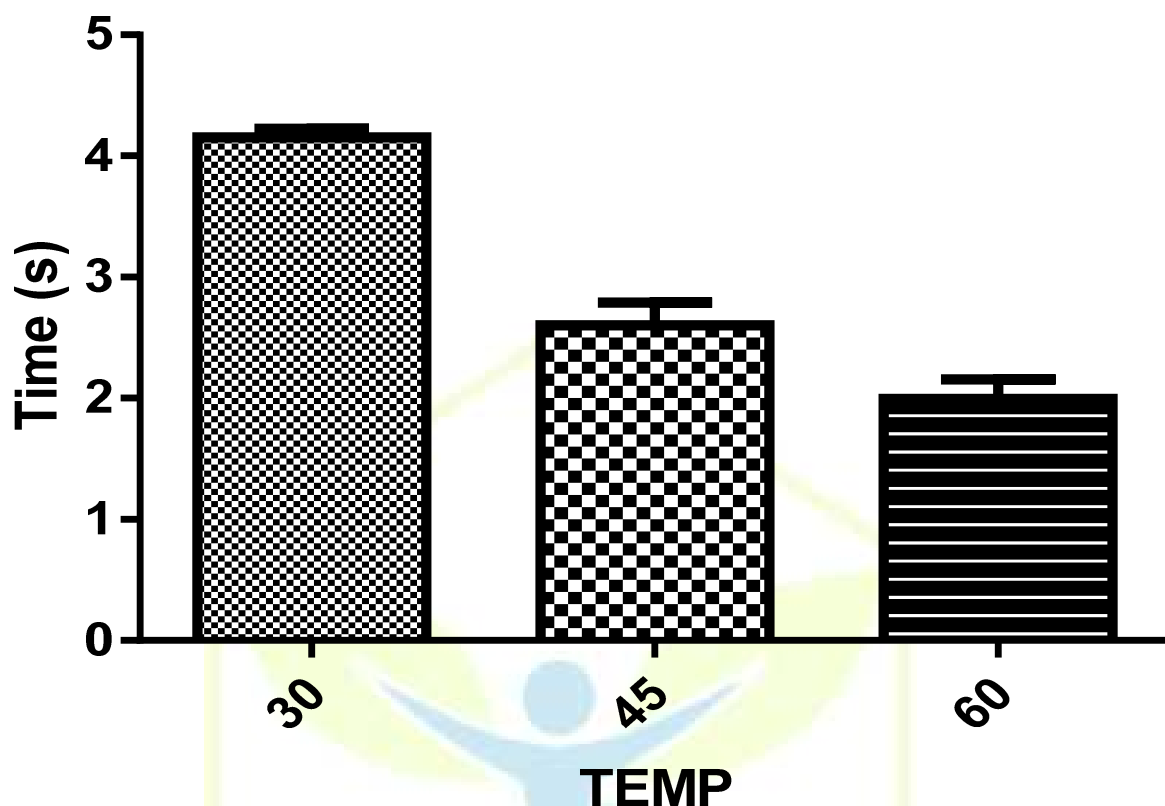


Figure 4: Graphical representation of the inhibition of thermally induced pain in Group D animals administered with 300mg/kg of methanol extract of *Artocarpus altilis*.

Table 5: Inhibition of thermally induced pain in Group E animals administered with 200mg/kg of Aspirin.

Parameter	Test Temperature (°C)		
	30	45	60
Percentage Protection (%)	2.18±0.174 ^b	1.22±0.059 ^{a, b}	1.35±0.127 ^a

Each value represents Mean ± SEM (standard error of mean) of five replicates of study animals. ^a represents significant difference at p<0.05 when comparing 30°C test temperature to others. ^b represents significant difference at p<0.05 when comparing 45°C test temperature to others.

Aspirin 200mg significantly (P<0.05) inhibited thermally induced pain at all the temperatures used in this study (between 30⁰c and 45⁰c, 30⁰c and 60⁰c). However it was not significant between temperature 45⁰c and 60⁰c.

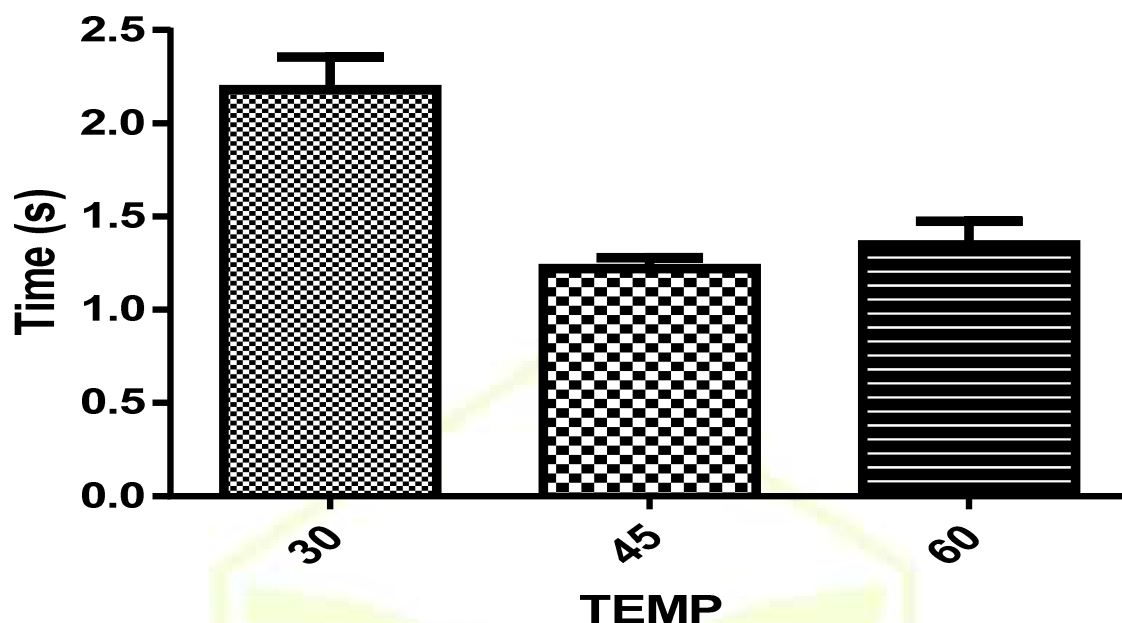


Figure 5: Graphical representation of the inhibition of thermally induced pain in Group E animals administered with 300mg/kg of methanol extract of *Artocarpus altilis*.

DISCUSSION

Artocarpusaltilis is known to contain a range of bio-active molecules which include tannins, phenolics, β -sitosterol, flavonoid, glycosides, saponins, gums and resins. These were revealed by the outcome of the phytochemical screening in this study and are in line with earlier reports.^[9, 10, 11] The pain relieving property of the plant in focus in the present study is more efficient in the seed of *Artocarpusaltilis* as most of the phytochemicals are believed to be present in greater abundance in them.^[12]

The outcome of the present investigation has shown that oral administration of *Artocarpusaltilis* has the potential to produce antinociception in rats in thermal

model of pain. The electric hot plate test is considered to be a suitable method for testing thermally induced pain and detecting strong analgesic pain.^[7] Methanol extract of *Artocarpusaltilis* was found to inhibit thermally induced pain in a dose dependent fashion. At a temperature of 60⁰c, the reaction time to 200mg/kg and 300mg/kg dose were most profound. In the same vein, however not surprisingly, the 100mg/kg was equally effective at all the various temperatures considered, thus, supposing that the antinociception properties of *Artocarpusaltilis* are not dependent on larger doses of the plant extract. Comparatively, it is important to note that antinociceptive qualities of the methanol extract of *Artocarpusaltilis* (100mg/kg, 200mg/kg and 300mg/kg) are highly similar to those

produced by Aspirin (200mg).

CONCLUSION

Thus, our findings in this study further confirm that *Artocarpusaltilis* at moderate non-lethal dose has strong anti-nociceptive activity. The overall outcome of this investigation suggest that methanol seeds extracts of *Artocarpusaltilis* contain bioactive constituents with analgesic activities, which further support the claims by folkloric users of the plant's ethnomedicinal properties and thus, the use of the plant in the management of painful conditions.

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